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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,328	LAL ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 26, 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *232-251* is/are pending in the application.

4a) Of the above claim(s) *243,244,250 and 251* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *232-242 and 245-249* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the paper filed January 26, 2004. Claims 1-231 have been canceled. Claims 232-251 have been added. Claims 243, 244, 250, and 251 have been withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected inventions. Claims 232-242 and 245-249 are currently under examination.

Applicants have requested that new Claims 243, 244, 250, and 251 be rejoined with the elected subject matter in accordance with *In re Ochiai*. The elected invention was drawn to the polypeptide comprising SEQ ID NO: 41. The original restriction was still deemed proper and final. However, in a telephonic interview on June 4, 2003, it was agreed that the methods of making the polypeptide and the method of using the polypeptide would be rejoined in accordance with *In re Ochiae* and in the spirit of unity of invention in this national stage application. The elected product is the polypeptide drawn to SEQ ID NO: 41, not the polynucleotides drawn to SEQ ID NO: 84. The Examiner has acted in good faith and has rejoined and examined the methods of making and using the polypeptide in the first action on the merits, even though the polypeptide was found to not be allowable in that action, in accordance with the telephonic agreement. Thus, Claims 243, 244, 250, and 251, which are drawn to methods of using the polynucleotides, will not be rejoined.

Applicants have filed a response (to an 8 page first action on the merits) that is approximately 720 pages. Many of these pages are art references relied on in their 48 page written response. None of these references have been placed on a PTO-1449. The Examiner will only address the art as Applicants have used them to support their arguments, and only their arguments will be addressed. It would not serve Applicants or the USPTO to place these references on a PTO-1449 and expect discussion or rebuttal of each because no one is doubting what Applicants have concluded from the teachings of the references. The arguments themselves are long and consuming due to the discussion of and buttressing by the references.

Thus, the Examiner has presented Applicants arguments as "topical", and she has tried to respond to the argument fully without diminishing or by-passing Applicants points. The intent is to stream-line the prosecution so that if Applicants choose to Appeal, the rejections are clear and the arguments from Applicants and from the Examiner are clear and concise.

Priority date is June 17, 1999.

Withdrawal of Objections and Rejections

The objection to the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code is withdrawn.

Maintenance of Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 247-249 (corresponding to canceled claims 19, 22, and 26) are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 247-249, it is not clear what activity is being assessed.

Applicants state that the specification provides the basis for the use of the terms. Please explain. The specification is not read into the claims. Applicants should particularly point out in the claim which specific activity will be assessed.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 232-242 and 245-249 (corresponding to canceled Claims 1-7, 9, 11, 16, 17, 19, 22, and 26) are again rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. Throughout the specification, the polypeptide having the amino acid sequence SEQ ID NO: 41 is stated to be a human transport protein, or TPPT-41 (page 10, line 34). The specification presents cloned DNA and the polypeptide sequence is deduced therefrom. Prophetic expressions systems are discussed at pages 70-71. A prophetic assay to demonstrate TPPT activity is discussed at page 71-72. No polypeptide having SEQ ID NO: 41 is in hand, and no assay determining its activity has been done. In Table 2 at page 87, the polypeptide having SEQ ID NO: 41 is stated to be homologous to myelin protein zero.

Goddard et al. (Pre-grant Pub US 2002/0192752) have in hand polypeptide PRO7425 having their designated SEQ ID NO: 12 which is identical to instant SEQ ID NO: 41. In Example 5, Goddard et al. demonstrate that PRO7425 stimulates the proliferation of T-lymphocytes 313% over CD4-IGG simulated control. Thus, while the instant specification discloses TPPT-41 as an intracellular transport protein based on deduced amino acid sequence homology to other transport proteins, the prior art teaches that this same protein is a extracellular-acting cytokine that stimulates the proliferation of T-cells.

Therefore, the instant invention lacks utility because the polypeptide TPPT-41, variants having 90% identity to SEQ ID NO: 41, biologically active and immunogenic active fragments thereof has been disclosed to be a transport protein or derived therefrom when this same protein has actually been shown to stimulate T lymphocyte proliferation. Thus, one skilled in the art could not use the polypeptide as disclosed. The polynucleotide encoding TPPT-41and polynucleotides having at least 70% identity to SEQ ID NO: 84 also lacks utility because the

polynucleotide has been taught to encode a transport protein. Further, the methods of using TPPT-41 for screening agonists, antagonists, or compounds that alter its activity lack utility because one could not perform the methods using the end-result disclosed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 242-242 and 245-249 (corresponding to canceled 1-7, 9, 11, 16, 17, 19, 22, and 26) are also again rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific, or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants urge (page 10, para. 1) that the polynucleotides can be used in toxicology testing, drug development, and in the diagnosis of disease. Further (para. 2 and 3) that the TPPT polypeptide has utility beyond reasonable probability required by law. The specification does not teach any toxin or drug to which the polynucleotides will be expressed. There is not disease set forth in which the polynucleotides will be used to diagnose. The TPPT polypeptide is not in hand and no specific activity has been shown for this polypeptide. Applicants have conjectured that the TPPT polypeptide will have myelin protein zero activity based on 36% identity to this protein. As noted in the utility rejection, Goddard et al. (Pre-grant Pub US 2002/0192752) have in hand polypeptide PRO7425 having their designated SEQ ID NO: 12 which is identical to instant SEQ ID NO: 41. In Example 5, Goddard et al. demonstrate that PRO7425 stimulates the

proliferation of T-lymphocytes 313% over CD4-IGG simulated control. Thus, while the instant specification discloses TPPT-41 as an intracellular transport protein based on deduced amino acid sequence homology to other transport proteins, the prior art teaches that this same protein is an extracellular-acting cytokine that stimulates the proliferation of T-cells. Thus, Applicants have provided conjecture, while the Examiner has provided hard evidence that the TPPT protein does not a myelin protein zero activity.

At page 10, para. 4 though page 12, Applicants discuss the declarations of Rockett, Iyer, and Bedilion. Applicants have provided declarations of Rockett, Iyer, and Bedilion and a host of references to support their view (which have not been provided on a PTO 1449).

Dr. Rockett discusses the importance of using polynucleotide and polypeptides expression profiling using a model of expression profile or a pattern of genes and protein expressed by treatment with known testicular toxins as standards, signatures, or fingerprints. Dr. Rockett's expertise and points are appreciated and well-taken. However, the specification does not establish any toxin which would induce the expression of SEQ ID NO: 41 or NO: 84 expression so that SEQ ID NO: 41 and NO: 84 can be a part of a pattern of expression in response to the toxin. Without this demonstration, the utility as a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not enough to say that SEQ ID NO: 41 or NO: 84 can be used in expression profiling; rather, in which toxin specific expression profile is SEQ ID NO: 41 or NO: 84 expressed?

Dr. Iyer discusses drug target validation and identity of secondary drug effects using expression profiling. Dr. Iyer's comments are well-taken. However, the specification does not establish any drug or pharmaceutical which would induce the expression of SEQ ID NO: 41 or NO: 84 expression so that SEQ ID NO: 41 and NO: 84 can be a part of a pattern of expression in response to the drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a drug is lost. It is not enough to say that SEQ ID NO: 41 or NO: 84 can be

used in expression profiling; rather, in which drug specific expression profile is SEQ ID NO: 41 or NO: 84 expressed?

Dr Bedilion discusses the commercial need of customers to have more and more genes on each array. The customers use the array as a research tool, that is, they expose the array comprising many polynucleotides or polypeptides to toxins or drugs and detect the resulting expression pattern. However, the specification does not establish any toxin or drug which would induce the expression of SEQ ID NO: 41 or NO: 84 expression so that SEQ ID NO: 41 and NO: 84 can be a part of a pattern of expression in response to the toxin or drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not enough to say that SEQ ID NO: 41 or NO: 84 can be used in expression profiling; rather, in which toxin or drug specific expression profile is SEQ ID NO: 41 or NO: 84 expressed?

At pages 12-15, 30-32, and 35-36, Applicants urge that the Examiner must accept their asserted utility. In most cases, the Examiner would agree. In this case, the Examiner has provided art that shows that Applicants polypeptide is an extracellular-acting cytokine that stimulates the proliferation of T-cells and not related to myelin protein zero and is not an intracellular transport protein.

At pages 15-29, 33-34, 36, and 37Applicants continue to argue that the polypeptide and polynucleotides can be used in toxicology testing and drug discovery, as well as diagnosis of disease. Again, as noted above, the specification does not teach any toxin or drug to which the polynucleotides or polypeptides will be expressed. There is no disease set forth in which the polynucleotides or polypeptides will be used to diagnose. Thus, Applicants cannot rely on these assertions to establish utility. One should not have to find out for themselves how to use the claimed polypeptides or polynucleotides.

At page 31, Applicants note that they have sold their sequences to databases and thus they have utility. The function is not know, and these data bases are used for further research as noted by Applicants statement that the polynucleotides are "powerful tools" and "for research uses".

At pages 37-49, Applicants state that the rejection should be overturned because it is based on the Revised Interim Utility Examination Guidelines. Applicants do not state that the Examiner has misapplied the Guidelines and therefore this line of argument is not germane to the rejection at hand.

It is noted that throughout their arguments Applicants refer to a variety of literature. These references will not be addressed because Applicants have not made them official on a PTO-1449.

Claims 232, 234, 235, 237, 241, 242, 245, and 247-249 (corresponding to cancelled Claims 1, 3, 6, 7, 9, 11, 16, 19, 22, and 26) are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Claims recite percent identities. The specification does not describe a functional polypeptide fragments or polypeptides having at least 90% identity to SEQ ID NO: 41, or a polypeptide having at least 90% identity to SEQ ID NO: 84 and having function. Therefore, the specification lacks written description for these variants.

Applicants arguments begin at pages 41-46. Applicants discuss structure but not function of the polypeptides and polynucleotides claimed. Example 14 of the Guidelines clearly states

that structure will be correlated with function to achieve written description. Thus, Applicants arguments are not persuasive.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 232-237, 242, 245, and 246 (corresponding to canceled Claims 1-4, 11, 16, and 17) are rejected under 35 U.S.C. 102(e) as being anticipated by Goddard et al. (Pre-grant Pub US 2002/0192752, priority to September 9, 1998). Goddard et al. teach polypeptide PRO7425 having their designated SEQ ID NO: 12 which is identical to instant SEQ ID NO: 41. Therefore, Goddard et al. teach a polypeptide comprising SEQ ID NO: 1 (Claim 232a), having at least 90% identity to SEQ ID NO: 41 (Claim 232b, 234), and comprising an immunogenic fragment of SEQ ID NO: 41 (Claim 232c). The PRO7425 is the same length as SEQ ID NO: 41; therefore, PRO7425 is a polypeptide that consists of SEQ ID NO: 41 (Claim 233). In Example 5, Goddard et al. demonstrate that PRO7425 stimulates the proliferation of T-lymphocytes 313% over CD4-IGG simulated control; thus, PRO7425 was placed in a pharmaceutical composition to perform this assay (Claims 245, 246)

SEQ ID NO: 11 of Goddard et al. encodes PRO7425 (Claims 235-237). SEQ ID NO: 11 shares 99.9% identity to instant SEQ ID NO: 84 and therefore shares at least 90% identity to SEQ ID NO: 84 (Claim 235-237, 242). The complements of SEQ ID NO: 11 (page 5, right col., para. 0057)

and RNA encoding SEQ ID NO: 41 are included in the definition of polynucleotide (page 9, right col., para. 0091)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 235-241 and 247-249 (corresponding to canceled Claims 4-7, 9, 19, 22, and 26) are again rejected under 35 U.S.C. 103(a) as being unpatentable over Goddard et al. (Pre-grant Pub US 2002/0192752, priority to September 9, 1998).

SEQ ID NO: 11 of Goddard et al. encodes PRO7425 (Claim 235, 236). SEQ ID NO: 11 shares 99.9% identity to instant SEQ ID NO: 84 and differs from SEQ ID NO: 84 by lacking the 3'C that is not involved in the coding or expression of PRO7425. Therefore, a polynucleotide consisting of SEQ ID NO: 84 is an obvious variant of SEQ ID NO: 11 disclosed by Goddard et al. because the 3' C does not contribute to the coding or expression of PRO7425 (Claim 235, 237, 238).

At Example 4, Goddard et al. notes that the clone from which PRO7425 is made has been deposited. Indeed, in Example 5, Goddard et al. demonstrate the activity of PRO7425 and therefore Goddard et al. must have recombinantly produced PRO7425 though Goddard et al. does not expressly teach how the PRO7425 was recombinantly produced. Goddard et al. provides many examples for the recombinant production of PRO polypeptides. The expression of PRO polypeptides in E. coli is discussed in Example 9, in mammalian cells in Example 10, in yeast in Example 11, and in insect cells in Example 12. After each of these examples, Goddard et al. states that "many of the PRO polypeptides disclosed herein were successfully expressed as

described above". Therefore, Example 10 will be used to exemplify the expression of PRO7425. In Example 10, Goddard et al. suggest that PRO polypeptides can be expressed in mammalian cells such as CHO cells. Goddard et al. suggests to place DNA encoding PRO polypeptides into expression vector PRK5 and transfect CHO cells with this vector. The cultures are incubated and the conditioned medium harvested and the expressed PRO concentrated and purified. Therefore, it would have been obvious to a person having ordinary skill in the art to place the nucleic acid having SEQ ID NO: 11 in to the expression vector PRK5 (Claim 239) and transfect CHO cells with this vector (Claim 240) and culture the CHO cells to express PRO7425 and harvest PRO7425 from the conditioned medium and purified the PRO7425 therefrom (Claim 241) because Goddard et al. suggest that these vectors, host cells, and methods of recombinant production are useful for the expression of PRO polypeptides including PRO7425. This recombinant technique for producing PRO7425 is predictable because Goddard et al. state that many of the PRO polypeptides disclosed herein were successfully expressed using this method.

At page 6, left column, para. 0064, Goddard et al. teach methods for identifying agonists and antagonists to a PRO polypeptide which comprises contacting the PRO polypeptide with a candidate molecule and monitor a PRO mediated biological activity. The agonist or antagonist would be useful in the preparation of a medicament for a condition that is responsive to PRO polypeptides (Page 6, top right col.). In Example 5, Goddard et al. teach a method fro stimulating T lymphocyte proliferation using PRO7425. Therefore, it would have been obvious to a person having ordinary skill in the art to perform a method for screening a compound for effectiveness as an agonist of PRO7425, said method comprising exposing a same comprising PRO7425 to the compound and determining an increase in T lymphocyte proliferation because Goddard et al. teach that this method would be useful for identifying agonists for the preparation of a medicament in the treatment of a condition responsive to PRO7425 (Claim 247,

249). It would have been obvious to a person having ordinary skill in the art to perform a method for screening a compound for effectiveness as an antagonist of PRO7425, said method comprising exposing a same comprising PRO7425 to the compound and determining a decrease in T lymphocyte proliferation because Goddard et al. teach that this method would be useful for identifying antagonists for the preparation of a medicament in the treatment of a condition responsive to PRO7425 (Claim 248, 249).

Applicants arguments begin at page 246. Applicants have filed the Declaration of inventors Yue and Baugn under 1.131 to overcome this rejection. The Declaration is defective because it is not signed by Yue.

New Rejections

Claims 232, 234, and 242 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims state that a polypeptide or a polynucleotides are at least 90% identical to SEQ ID NO: 41 or NO: 84. The term "identical" is unvaried, that is, one this is either identical to another or it is not. Thus, a polypeptide or polynucleotides can not be 90% identical to another polypeptide or polynucleotides, respectively. The term --- identity – should be used.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER